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8/30/10



Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Previously presented) An antibody comprising a single-chain polypeptide that binds to the thrombopoietin (TPO) receptor (Mpl), wherein said antibody comprises two heavy chain variable regions and two light chain variable regions, and at least one of the heavy chain variable regions comprises a set of CDR1, CDR2 and CDR3 sequences selected from the group consisting of:

(a) SEQ ID NOs: 27, 28, and 29;

(b) SEQ ID NOs: 36, 37, and 38; and

(c) SEQ ID NOs: 57, 58, and 59.

2. (Previously presented) The antibody of claim 1, wherein the two heavy chain variable regions and the two light chain variable regions are arranged in the order, from the N-terminus of the single-chain polypeptide, of heavy chain variable region, light chain variable region, heavy chain variable region, and light chain variable region.

3. (Previously presented) The antibody of claim 1, wherein the four variable regions are linked by linkers.

4. (Previously presented) The antibody of claim 3, wherein each linker comprises 15 amino acids.

5. (Canceled)

6. (Previously presented) The antibody of claim 1, which is a humanized antibody.

7. (Canceled)

8. (Previously presented) The antibody of claim 1, wherein the antibody binds to soluble Mpl.

9. – 10. (Canceled)

11. (Previously presented) The antibody of claim 1, wherein the antibody binds to soluble Mpl with a KD = $10^{-6}$ M or lower.

12. (Previously presented) The antibody of claim 1, wherein the antibody binds to soluble Mpl with a KD = $10^{-7}$ M or lower.

13. (Previously presented) The antibody of claim 1, wherein the antibody has a TPO agonistic activity of EC50 = 100 nM or lower.

14. (Previously presented) The antibody of claim 1, wherein the antibody has a TPO agonistic activity of EC50 = 30 nM or lower.

15. (Previously presented) The antibody of claim 1, wherein the antibody has a TPO agonistic activity of EC50 = 10 nM or lower.

16. (Canceled)

17. (Previously presented) The antibody of claim 1, wherein at least one of the light chain variable regions comprises a set of CDR1, CDR2 and CDR3 sequences selected from the group consisting of:

(a) SEQ ID NOs: 84, 85, and 86;

(b) SEQ ID NOs: 93, 94, and 95; and

(c) SEQ ID NOs: 114, 115, and 116.

18. (Currently amended) The antibody of claim 1 comprising any one of:

(a) heavy chain variable region CDR1, CDR2, and CDR3 comprising amino acid sequences consisting of SEQ ID NOs: 27, 28, and 29, respectively, and light chain variable region CDR1, CDR2, and CDR3 comprising amino acid sequences consisting of SEQ ID NOs: 84, 85, and 86, respectively;

(b) heavy chain variable region CDR1, CDR2, and CDR3 comprising amino acid sequences consisting of SEQ ID NOs: 36, 37, and 38, respectively, and light chain variable region CDR1, CDR2, and CDR3 comprising amino acid sequences consisting of SEQ ID NOs: 93, 94, and 95, respectively; and

(c) heavy chain variable region CDR1, CDR2, and CDR3 comprising amino acid sequences consisting of SEQ ID NOs: ~~9, 10, and 11~~57, 58 and 59, respectively, and light chain variable region CDR1, CDR2, and CDR3 comprising amino acid sequences consisting of SEQ ID NOs: 114, 115, and 116, respectively.

19. – 22. (Canceled)

23. (Previously presented) The antibody of claim 1, wherein at least one of the heavy chain variable regions comprises a set of FR1, FR2, FR3, and FR4 sequences selected from the group consisting of:

(a) SEQ ID NOs: 230, 232, 234, and 236; and

(b) SEQ ID NOs: 265, 267, 269, and 271.

24. (Previously presented) The antibody of claim 1, wherein at least one of the light chain variable regions comprises a set of FR1, FR2, FR3, and FR4 sequences selected from the group consisting of:

(a) SEQ ID NOs: 239, 241, 243, and 245; and

(b) SEQ ID NOs: 272, 274, 276, and 278.

25. (Previously presented) The antibody of claim 1, comprising any one of:

(a) heavy chain variable region FR1, FR2, FR3, and FR4 comprising amino acid sequences consisting of SEQ ID NOs: 230, 232, 234, and 236, respectively, and light chain variable region FR1, FR2, FR3, and FR4 comprising amino acid sequences consisting of SEQ ID NOs: 239, 241, 243, and 245, respectively; and

(b) heavy chain variable region FR1, FR2, FR3, and FR4 comprising amino acid sequences consisting of SEQ ID NOs: 265, 267, 269, and 271, respectively, and light chain variable region FR1, FR2, FR3, and FR4 comprising amino acid sequences consisting of SEQ ID NOs: 272, 274, 276, and 278, respectively.

26. (Previously presented) The antibody of claim 1, wherein at least one of said heavy chain variable regions comprises the amino acid sequence of SEQ ID NO: 140, 162, or 229.

27. (Previously presented) The antibody of claim 1, wherein at least one of said light chain variable regions comprises the amino acid sequence of SEQ ID NO: 141, 163, or 238.

28. (Previously presented) The antibody of claim 1, wherein:

(a) at least one of the heavy chain variable regions comprises the amino acid sequence of SEQ ID NO: 229, and at least one of the light chain variable regions comprises the amino acid sequence of SEQ ID NO: 238;

(b) at least one of the heavy chain variable regions comprises the amino acid sequence of SEQ ID NO: 140, and at least one of the light chain variable regions comprises the amino acid sequence of SEQ ID NO: 141; or

(c) at least one of the heavy chain variable regions comprises the amino acid sequence of SEQ ID NO: 162, and at least one of the light chain variable regions comprises the amino acid sequence of SEQ ID NO: 163.

29. – 31. (Canceled)

32. (Previously presented) The antibody of claim 1, wherein the antibody recognizes an epitope within the region of amino acids 26 to 274 of human Mpl (SEQ ID NO: 123).

33. (Previously presented) The antibody of claim 1, which has TPO agonistic activity.

34. -37. (Canceled)

38. (Previously presented) A pharmaceutical composition comprising the antibody of claim 32.

39. -43. (Canceled)

44. (Previously presented) A method of treating or reducing the incidence of thrombocytopenia in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the pharmaceutical composition of claim 38.

45. (Previously presented) A method for increasing platelet number in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the pharmaceutical composition of claim 38.

46. (Previously presented) The method of claim 45, wherein the pharmaceutical composition is administered to the subject after the administration of platelet components to the subject.

47. (Previously presented) A method for increasing the amount of platelet components at the time of blood collection, the method comprising preadministering to a blood collection subject an effective amount of the pharmaceutical composition of claim 38.

48. (Previously presented) The method of claim 47, further comprising collecting blood from the subject after said preadministration.